

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 June 2002 (27.06.2002)

PCT

(10) International Publication Number
WO 02/50144 A2

(51) International Patent Classification⁷: C08F 230/08

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(21) International Application Number: PCT/US01/46500

(22) International Filing Date: 3 December 2001 (03.12.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/256,712 19 December 2000 (19.12.2000) US

(71) Applicant: BAUSCH & LOMB INCORPORATED
[US/US]; One Bausch & Lomb Place, Rochester, NY
14604-2701 (US).

(72) Inventors: BONAFINI, Jr., James, A.; 15 Park View
Drive, Pittsford, NY 14604-2701 (US). SALAMONE,
Joseph, C.; 740 NW 6th Street, Boca Raton, FL 33486
(US).

(74) Agents: POLYN, Denis, A. et al.; One Bausch & Lomb
Place, Rochester, NY 14604-2701 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI,

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG).

Declaration under Rule 4.17:

— as to the identity of the inventor (Rule 4.17(i)) for the fol-
lowing designations AE, AG, AL, AM, AT, AU, AZ, BA, BB,
BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK,
DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent
(GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG)

Published:

— without international search report and to be republished
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: POLYMERIC BIOMATERIALS CONTAINING SILSESQUIXANE MONOMERS

(57) Abstract: The invention provides a biocompatible copolymer produced by polymerizing a mixture comprising at least one monomer selected from the group consisting of itaconates, (meth)acrylates, fumarates and styrenics, at least one ethylenically unsaturated organosiloxane monomer and at least one monomer comprising a POSS compound.

WO 02/50144 A2

BEST AVAILABLE COPY

POLYMERIC BIOMATERIALS CONTAINING SILSESQUIOXANE MONOMERS

BACKGROUND OF THE INVENTION

This invention relates to improved copolymers useful as biocompatible materials. Specifically, this invention relates to copolymers useful as ophthalmic lenses, for example, contact lenses.

Early hard contact lenses were produced from polymethyl methacrylate (PMMA) or cellulose acetate butyrate (CAB). Rigid, gas permeable (RGP) contact lenses formed of silicone-containing copolymers offered various advantages over PMMA and CAB lenses (particularly increased oxygen permeability). Another example of an RGP material is a copolymer comprising a silicone-containing monomer and methyl methacrylate.

A newer class of copolymers for silicone-containing RGP lenses is itaconate ester copolymers. U.S. Pat. Nos. 4,152,508 (Ellis et al.), 4,330,383 (Ellis et al.) and 4,826,889 (Ellis et al.) disclose copolymers for contact lenses prepared from: a monofunctional siloxanyl ester monomer; an itaconate ester; an ester of a monohydric or polyhydric alkanol or phenol and a (meth)acrylic acid; a crosslinking agent; and preferably a hydrophilic monomer.

Known copolymers for RGP lenses also include copolymers of fluorinated itaconate esters, such as the copolymers disclosed in U.S. Pat. Nos. 4,686,267 (Ellis et al.) and 4,996,275 (Ellis et al.), which are prepared from a fluorinated itaconate ester and an ethylenically unsaturated organosiloxane.

Other examples of itaconate ester copolymers for RGP lenses are disclosed in the following U.S. Pat. Nos. 4,602,074 (Mizutani et al.); 4,508,884 (Wittmann et al.); 4,743,667 (Mizutani et al.); 4,826,936 (Ellis); and 4,861,850 (Novicky).

As disclosed in U.S. Pat. No. 4,152,508, the itaconate ester provides rigidity,

hardness and some degree of wettability to the resultant copolymer. But the inclusion of an itaconate ester tends to make the resultant copolymers more brittle. This illustrates a major challenge in the development of new ophthalmic lens materials: that adding a given monomer to a polymer mix with the goal of attaining a particular characteristic may inherently include other less desirable characteristics. For example, silicone-containing monomers may desirably contribute rigidity, while undesirably decreasing toughness.

Certain multifunctional organosiloxanes have been described as useful for adding higher impact strength and reducing brittleness of itaconate RGP copolymers. U.S. Pat. No. 4,826,936 describes a class of multifunctional organosiloxanes having such properties.

Silsesquioxane macromers are silicon-containing cage molecules based upon the structure of oxygen and silicon tetrahedrons. Silsesquioxane macromers can be polymerized to produce heat-resistant materials such as high-temperature plastics. Examples of silsesquioxane-containing materials are disclosed in U.S. Patents 5,412,053; 5,484,867; and 5,589,562 (all to Lichtenhan et al.). While bulky materials containing silicon and oxygen have been of interest to improve the oxygen permeability of biocompatible materials such as contact lens materials, those materials are markedly different than the heat-resistant materials that are the subject of ongoing research relating to silsesquioxane macromers.

Thus it would be desirable to improve the oxygen permeability of biocompatible materials without sacrificing other essential properties. In particular, it would also be desirable to provide a biocompatible material that is optically clear, and also has excellent machinability and toughness.

SUMMARY OF THE INVENTION

The present invention relates to silsesquioxane-containing copolymers that are useful as biocompatible materials. The copolymers of the invention are the polymerization product of a mixture comprising:

- (a) a monomer selected from the group consisting of itaconates, (meth)acrylates, fumarates and styrenes;
- (b) an ethylenically unsaturated organosiloxane monomer; and
- (c) a POSS compound containing at least one substituent group comprising a polymerizable activated unsaturated group.

The monomers useful for polymerizing with POSS compounds in accordance with the invention include any ethylenically unsaturated monomer, for example, alkyl methacrylates such as methyl methacrylate and neopentyl methacrylate, as well as aromatic methacrylates such as benzyl methacrylate.

Halogenated methacrylates and itaconates are also useful monomers in the present invention. Examples include fluoroalkyl methacrylates such as hexafluoroisopropyl methacrylate and trifluoroethyl methacrylate, and halogenated itaconates such as bis (1,1,1,3,3,3-hexafluoro-2-propyl) itaconate.

Aromatic ring compounds may also be useful as monomers in the present invention. Examples of suitable aromatic monomers include alkyl substituted styrenes such as t-butyl styrene. Other useful monomers include vinyl lactams and n-vinyl pyrrolidone.

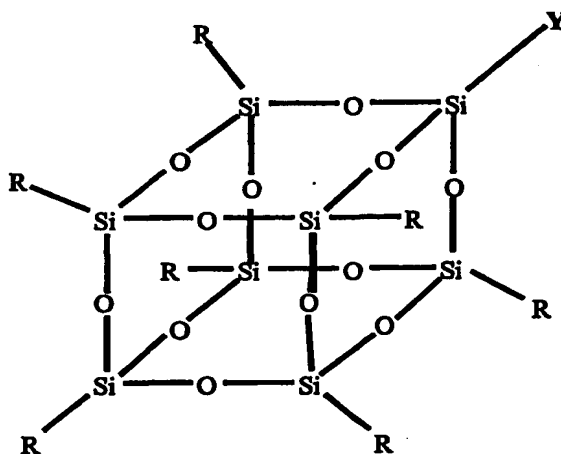
Hydrophilic monomers such as (meth)acrylic acid and (meth) acrylamides such as N,N-dimethylacrylamide are also useful in the invention.

Monomers useful in the present invention may also contain two or more functional groups of the type listed above.

DETAILED DESCRIPTION OF THE INVENTION

The materials of the present invention contain functionalized monomers based upon silsesquioxane ("POSS") compounds. The POSS compounds useful as monomers in accordance with the invention can be produced by general methods known in the art, such as the methods disclosed in U.S. Pat. Nos. 5,412,053; 5,484,867; and 5,589,562 (all to Lichtenhan et al.).

The general cage structure of one example of a silsesquioxane-based monomeric unit is shown below as Structure (I).



(I)

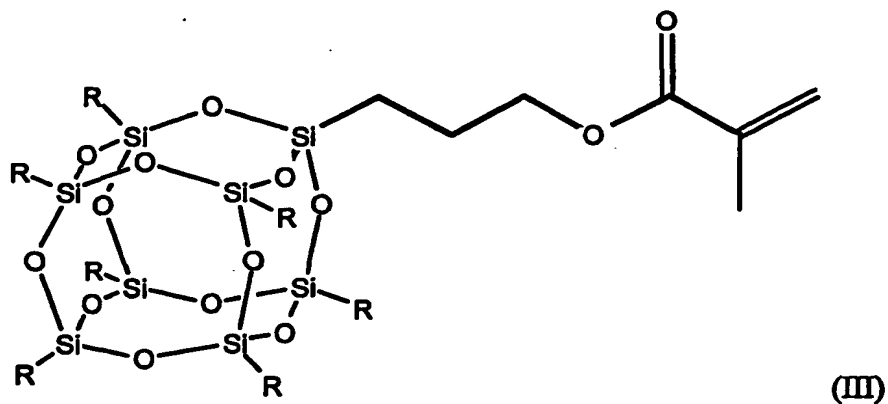
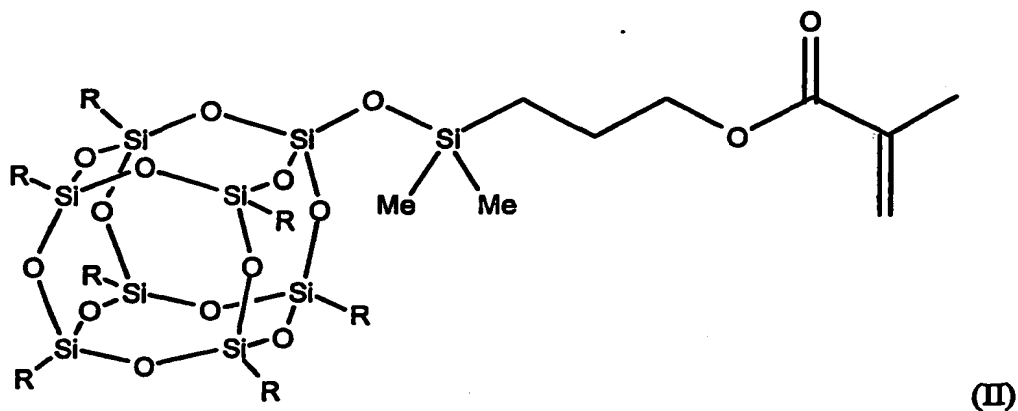
wherein:

each Y is independently an activated unsaturated radical; and

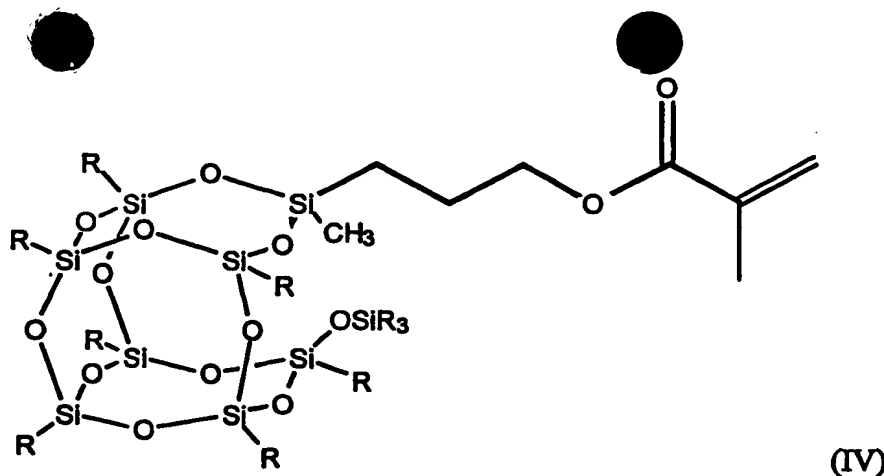
each R is independently selected from the group consisting of a C₁-C₁₂ monovalent hydrocarbon radical, a C₁-C₁₂ monovalent hydrocarbon radical containing ether linkages, a halogen-substituted C₁-C₁₂ monovalent hydrocarbon radical, and a halogen-substituted C₁-C₁₂ monovalent hydrocarbon radical containing ether linkages.

Silsesquioxane-based polymers useful in the present invention may have smaller or large cage sizes than the structure shown above, and may also comprise closed or open cage structures.

The silsesquioxane-based polymers useful in the invention must contain at least one polymerizable site, preferably an ethylenically unsaturated site. Structures (II) and (III) illustrate examples of suitable closed-cage monomers. Structure III represents a preferred monomer.



The polymers of the invention may further include one or more open-cage monomers as shown below by Structure (IV).



The term “polyhedral oligomeric silsesquioxane” or “POSS” as used herein describes a type of three-dimensional siloxane molecule in which at least two siloxane rings form a rigid molecular structure. Both open-cage and closed cage POSS monomers are useful in the present invention.

The term “closed-cage POSS monomer” means a polyhedral oligomeric silsesquioxane monomer in which each ring-member silicon atom is linked to three other ring-member silicon atoms through oxygen atoms.

The term “open-cage POSS monomer” means a polyhedral oligomeric silsesquioxane monomer in which at least two silicon atoms are each linked to no more than two other ring-member silicon atoms through oxygen atoms.

The polymers of the invention may optionally contain a hydrophilic monomer.

The materials of the invention are biocompatible. The materials are particularly useful as rigid gas permeable (RGP) contact lens materials due to their improved toughness, oxygen permeability and flexure resistance.

In accordance with the invention, it has been found that POSS compounds are especially effective in improving the oxygen permeability and flexure resistance of biocompatible polymeric materials.

Polysilsesquioxanes (POSS materials) are represented by the formula $[\text{RSiO}_{1.5}]_{\lambda}$ where λ = molar degree of polymerization and R = organic substituent (H, siloxy, cyclic or linear aliphatic or aromatic groups that may additionally contain reactive functionalities such as alcohols, esters, amines, ketones, olefins, ethers or halides). Polysilsesquioxanes may be either homoleptic or heteroleptic. Homoleptic systems contain only one type of R group while heteroleptic systems contain more than one type of R group.

POSS and POS nanostructure compositions are represented by the formula:

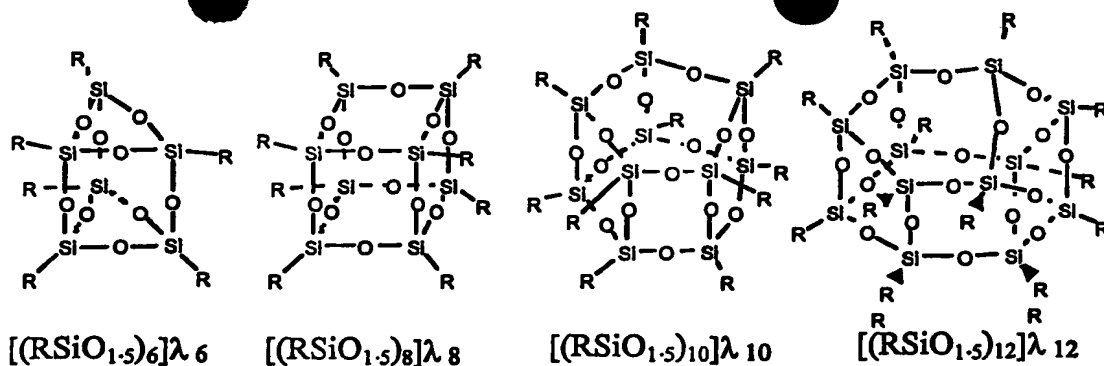
$[(\text{RSiO}_{1.5})_n]_{\lambda\#}$ for homoleptic compositions;

$[(\text{RSiO}_{1.5})_m(\text{R}'\text{SiO}_{1.5})_n]_{\lambda\#}$ for heteroleptic compositions (where $\text{R} \neq \text{R}'$); and

$[(\text{RSiO}_{1.5})_m(\text{RXSiO}_{1.0})_n]_{\lambda\#}$ for functionalized heteroleptic compositions (where R groups can be equivalent or inequivalent).

In all of these formulae, R is the same as defined above for Structure (I) and X includes but is not limited to OH, Cl, Br, I, alkoxide (OR), acetate (OOCR), peroxide (OOR), amine (NR_2), isocyanate (NCO), and R. The symbols m and n refer to the stoichiometry of the composition. The symbol λ indicates that the composition forms a nanostructure and the symbol # refers to the number of silicon atoms contained within the nanostructure. The value for # is usually the sum of $m+n$. It should be noted that $\lambda\#$ is not to be confused as a multiplier for determining stoichiometry, as it merely describes the overall nanostructural characteristics of the system (also referred to as "cage size").

Structures (V) through (VIII), below, illustrate examples of a POSS monomers in which $\lambda = 6, 8, 10$ and 12 , respectively.



The POSS monomer is preferably employed at 5 to 60% by weight of the monomeric mixture from which the copolymer is prepared in order to provide copolymers having sufficient rigidity and hardness. According to preferred embodiments, the POSS monomer is present at 20 to 85 weight percent, with 30 to 65 weight percent being more preferred, in the monomeric mixture.

The itaconates are known in the art and include compounds of structure (IX):



wherein X and Y, which may be the same or different, are independently: hydrogen; C₁-C₁₈ alkyl or fluoro-substituted alkyl groups; C₅-C₁₈ cycloalkyl or fluoro-substituted alkyl groups; C₂-C₆ alkenyl groups or fluoro-substituted alkenyl groups; phenyl groups or fluoro-substituted phenyl groups; benzyl or fluoro-substituted benzyl groups; phenethyl or fluoro-substituted phenethyl groups; or C₂-C₁₈ ether or fluoro-substituted ether groups; provided that at least one of X and Y is other than hydrogen.

Representative meth(acrylates) include esters of C₁-C₂₀ monohydric or polyhydric alkanol or phenol and (meth)acrylic acid. Representative meth(acrylate) monomers include: alkyl (meth)acrylates, such as methyl methacrylate, ethyl methacrylate, and neopentyl methacrylate; cycloalkyl-containing (meth)acrylates, such as cyclohexyl methacrylate; and phenyl methacrylate. This (meth)acrylate may be included in the monomeric mixture at 0 to about 50 weight percent, more preferably at about 5 to about 35 weight percent.

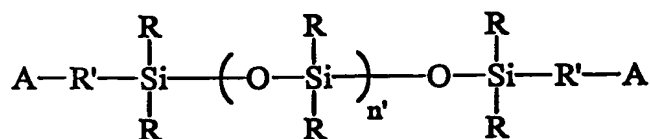
Itaconates may be used to partially or completely replace meth(acrylate) compounds in the present invention. Representative itaconates include methyl itaconate, dimethyl itaconate, phenyl itaconate, methyl phenyl itaconate, bis (1,1,1,3,3,3-hexafluoro-2-propyl) itaconate, bis (2,2,2-trifluoroethyl) itaconate, bis (1H,1H-perfluorooctyl) itaconate, bis (1H,1H,1H-perfluoroundecyl) itaconate, bis (perfluoro-t-butyl) itaconate, bis (pentafluorophenyl) itaconate, bis (2H,2H-perfluorobenzyl) itaconate, and bis (pentafluorophenylmethyl) itaconate.

Itaconates may comprise up to 60% by weight of the monomeric mixture from which the copolymer is prepared in order to provide copolymers having sufficient rigidity and hardness. If itaconates are included in the monomer mixture, they are typically present in concentrations of 20 to 55 weight percent, preferably 30 to 50 weight percent.

As recognized in the art, when an itaconate is used in place of, or in combination with, methyl methacrylate, the resultant copolymer has increased rigidity and hardness. However, the inclusion of the itaconate ester also tends to make the resultant copolymer more brittle. RGP contact lens materials are frequently provided in the form of rods, buttons, or lens blanks, which are subsequently machined into contact lenses having desired lens surfaces. When the copolymeric material is brittle, difficulties can be encountered in machining such materials, such as chipping or flaking or even breakage of the material.

In accordance with the invention, it has been found that POSS monomers can effectively toughen the resultant copolymer, thereby overcoming the disadvantages attributed to the itaconate monomer. The copolymers represent improved itaconate-containing RGP materials having optical clarity, reduced brittleness, and improved toughness. Preferably, the POSS-containing polymers have a toughness of at least about 1.2 MPa.mm/mm (as determined by ASTM D 790M-86 standards), and more preferably, a toughness of at least about 1.5 MPa.mm/mm.

Multifunctional organosiloxanes have been described as useful in contact lens formulations, including siloxane compounds of the general formula shown below as Structure (XI).



(XI)

(wherein A, R' and R generally correspond to the definitions given for formula (II), and n' has various ranges), Applicants have found that for POSS-containing contact lens materials, it is preferred to include an organosiloxane monomer.

In a preferred embodiment, the organosiloxane compound has the structure shown above as Structure (XI), and n averages at least about 15.

In Structure (XI), A is an activated unsaturated radical, i.e., an unsaturated group that includes a substituent for facilitating free radical polymerization, preferably a vinyl-containing substituent. Representative A radicals include (meth)acryloxy, (meth)acrylamido and styryl. (As used herein, the term "(meth)" denotes optional methyl substitution. Thus, a term such as "(meth)acrylate" denotes "acrylate or methacrylate".) The methacryloxy radical is more preferred.

Each R' is independently a C₁-C₂₂ divalent hydrocarbon radical. Representative R' radical include alkylene radicals, and preferred radicals include methylene, propylene and butylene.

Each R is independently selected from the group consisting of a C₁-C₁₂ monovalent hydrocarbon radical, a C₁-C₁₂ monovalent hydrocarbon radical containing ether linkages, a halogen-substituted C₁-C₁₂ monovalent hydrocarbon radical, and a halogen-substituted C₁-C₁₂ monovalent hydrocarbon radical containing ether linkages. Representative R radicals include alkyl, cycloalkyl, aryl, aralkyl, alkaryl radicals, alkoxyalkyl radicals, and halogen-substituted derivatives thereof. Preferred radicals include C₁-C₄ alkyl, with methyl being especially preferred.

The siloxane compound is employed in an amount effective to reduce the brittleness of the resultant copolymer. Generally, the siloxane compound should be present at about 3 to about 25 weight percent of the initial monomeric mixture, more preferably at about 5

to about 20 weight percent, with about 9 to about 15 weight percent being especially preferred. One skilled in the art can readily determine optimal amounts for specific formulations.

The ethylenically unsaturated organosiloxane monomer (exclusive of the POSS compound) is useful for increasing oxygen permeability of the copolymer. Preferred organosiloxanes are monofunctional organosiloxane containing a (meth)acrylate radical, such as tris(trimethylsiloxy)methacryloxypropylsilane, pentamethyldisiloxanylmethyl methacrylate, heptamethylcyclotetrasiloxanepropyl methacrylate, heptamethylcyclotetrasiloxanemethyl methacrylate and methyl-di(trimethylsiloxy)methacryloxymethylsilane. Other organosiloxane monomers known in the art are described in U.S. Pat. No. 4,686,267, the disclosure of which is incorporated herein by reference. The organosiloxane monomer may be included in the monomeric mixture at about 2 to about 60 weight percent, more preferably at about 5 to about 50 weight percent.

A hydrophilic monomer may be added to the reaction mixture for increasing hydrophilicity and improving wettability of the resultant copolymer. Conventional hydrophilic monomers include: hydrophilic (meth)acrylates, such as 2-hydroxyethyl methacrylate; hydrophilic (meth)acrylamides, such as methacrylamide and N,N-dimethylacrylamide; (meth)acrylic carboxylic acids, such as methacrylic acid; and vinyl lactams, such as N-vinylpyrrolidone. The hydrophilic monomer may be included in the monomeric mixture at about 1 to about 25 weight percent, more preferably at about 3 to about 15 weight percent.

Other materials known for contact lens formulations can be employed in the monomeric mixture from which the itaconate copolymer is prepared.

A (meth)acrylate monomer may be included which further modifies hardness of the copolymer. Such monomers are preferably an ester of a C₁-C₂₀ monohydric or polyhydric alkanol or phenol and (meth)acrylic acid. Representative monomers include: alkyl (meth)acrylates, such as methyl methacrylate, ethyl methacrylate, and neopentyl methacrylate; cycloalkyl-containing (meth)acrylates, such as cyclohexyl methacrylate;

and phenyl methacrylate. This (meth)acrylate may be included in the monomeric mixture at 0 to about 50 weight percent, more preferably at about 5 to about 35 weight percent.

A conventional non-silicone containing crosslinking agent may be employed. Crosslinking agents include polyfunctional derivatives of (meth)acrylic acid, (meth)acrylamide and other multi-vinyl substituted compounds. Representative crosslinking agents include: ethylene glycol dimethacrylate, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, tetraethylene glycol dimethacrylate, neopentyl glycol dimethacrylate, trimethylolpropane trimethacrylate, hexamethylene bisacrylamide and divinyl benzene. The crosslinking agent may be included in the monomeric mixture at 0 to about 20 weight percent, more preferably at about 1 to about 10 weight percent.

Accordingly, preferred copolymers are prepared from a monomeric mixture comprising:

- (a) an itaconate ester at about 0 to about 60 weight percent, preferably about 20 to about 55 weight percent;
- (b) a POSS compound (I) at about 3 to about 85 weight percent, preferably about 5 to about 60 weight percent, and more preferably about 10 to about 25 weight percent;
- (c) a siloxane compound of formula (II) at about 3 to about 25 weight percent, preferably about 5 to about 20 weight percent, and more preferably about 9 to about 15 weight percent;
- (d) an ethylenically unsaturated organosiloxane monomer at about 2 to about 60 weight percent, preferably about 5 to about 50 weight percent;
- (e) a hydrophilic monomer at about 1 to about 25 weight percent, preferably about 3 to about 15 weight percent;
- (f) a (meth)acrylate monomer at 0 to about 50 weight percent, preferably about 5 to about 35 weight percent; and

(g) a crosslinking agent at 0 to about 20 weight percent, preferably about 1 to about 10 weight percent.

Other optional components include conventional free radical initiators, which are generally employed at 0.01 to 2% by weight, and coloring agents.

The monomeric mixtures can be polymerized by methods known in the art, preferably in the presence of heat or ultraviolet radiation, and if desired, the copolymers can be treated with gamma radiation to reduce any unreacted monomers. Preferably, the mixtures are molded in a shape which is subsequently machined into the form of a contact lens, such as rod stock, a lens button, or a lens blank containing one finished surface. Alternately, the mixtures can be molded directly in the form of a contact lens.

EXAMPLES

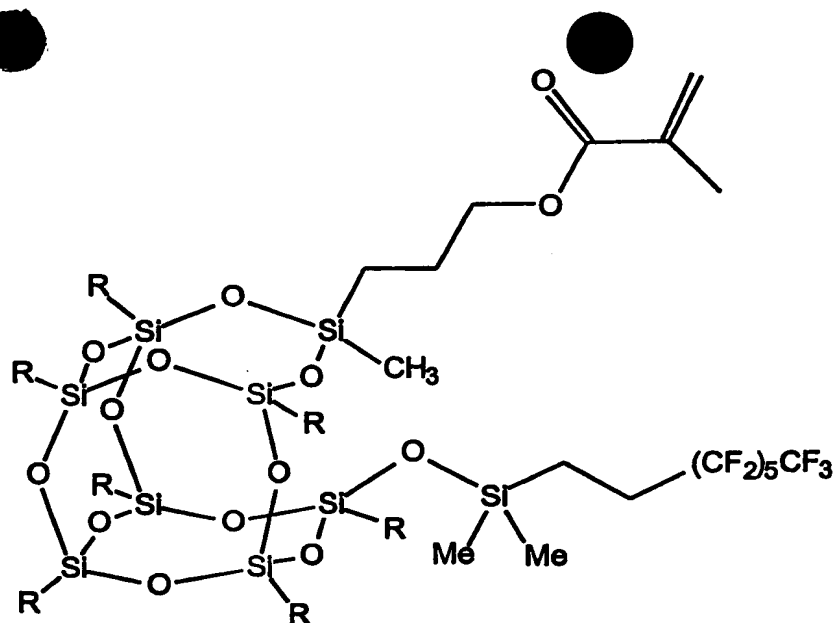
The following examples further illustrate preferred embodiments of the invention.

Various copolymers were polymerized from the monomeric mixtures listed in the following tables, wherein the amounts of the individual components are given in parts by weight. The mixtures were placed in cylindrical tubes, and the tubes were deoxygenated and sealed. The mixtures were polymerized by heating in a water bath (40° C. for 3 days), followed by heating in an oven (65° C. for 2 days). Various copolymers were subjected to post-polymerization treatment to reduce unreacted monomers, including exposure to gamma radiation in an inert atmosphere.

Toughness and modulus were determined according to ASTM-D 790M-86 standards on 0.5-mm disk samples cut from the polymerized rods. Standard deviation is listed parenthetically in the tables. Permeability was determined on 0.5-mm disk samples in accordance with ANSI Z80.20 and ISO 9913-1.2:1996 "Determination of Oxygen Permeability and Transmissibility with the FATT Method".

The results are summarized in the following tables, which include the following abbreviations:

1. POSS - (Polyhedral Oligomeric Silsesquioxane) where R is cyclopentyl or isobutyl.
2. AIBN - 2,2-azobisisobutyronitrile (initiator).
3. AIVN - 2,2-azobisisovaleronitrile (initiator).
4. BHI - bis(1,1,1,3,3,3-hexafluoro-2-propyl) itaconate.
5. MAA - methacrylic acid.
6. MMA - methyl methacrylate.
7. NPGDMA - neopentyl glycol dimethacrylate.
8. NPMA - neopentyl methacrylate.
9. NVP - N-vinylpyrrolidone.
10. TRIS - tris(trimethylsiloxy)silylpropyl methacrylate.
11. HFIPM - hexafluoroisopropyl methacrylate.
12. M_2D_{25} - Formula (I) wherein each R is methyl, each R' is butylene, each A is methacrylate, and n averages about 25.



R = cyclopentyl or butyl

Structure XII

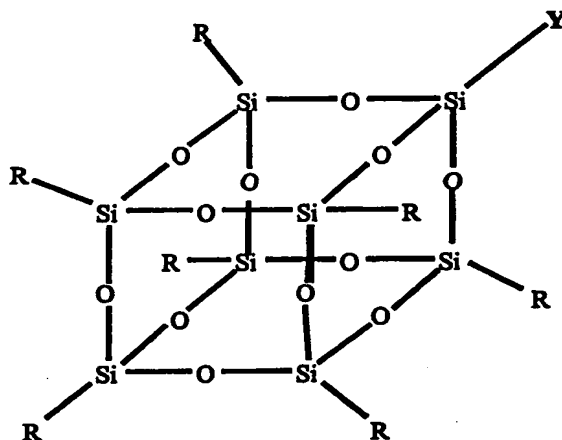
Example No.	1	2	3
Constituent			
MMA	2.5	2.5	2.5
MAA	5.5	5.5	5.5
t-butyl styrene	38.9	38.9	38.9
POSS (See Structure 12 where R is cyclopentyl)	28.5	19.1	9.4
TRIS	0	9.4	19.1
M ₂ D ₂₅	11.5	11.5	11.5
NPGDMA	7	7	7
NVP	6.1	6.1	6.1
AIVN	0.062	0.062	0.062
AIBN	0.19	0.19	0.19
FD&C GREEN #6	0.00979	0.00979	0.00979
UV Absorber	0.3	0.3	0.3
TOTAL	100	100	100
Physical Properties			
Rockwell Hardness	114	113	115
Refractive Index	1.500	1.498	1.495
Specific Gravity	1.12	1.11	1.04
Dk ISO/FATT	17	23	34
Modulus (Mpa)	1649	1566	1177
Toughness (MPA.mm/mm)	3.85	3.09	3.27

The data summarized in the above table demonstrate that the POSS compounds of the invention produce optically clear materials having sufficient oxygen permeability and toughness to be suitable for use as RGP contact lens materials.

Although certain preferred embodiments have been described, it is understood that the invention is not limited thereto and modifications and variations would be evident to a person of ordinary skill in the art.

We claim:

1. A biocompatible copolymer produced by polymerizing a mixture comprising:
 - (a) at least one monomer selected from the group consisting of itaconates, (meth)acrylates, fumarates and styrenics;
 - (b) at least one monomer comprising a POSS compound.
2. The copolymer of claim 1 further comprising an ethylenically unsaturated organosiloxane monomer.
3. The biocompatible copolymer of claim 1 wherein said POSS compound has the formula:



wherein:

each Y is independently an activated unsaturated radical; and

each R is independently selected from the group consisting of a C₁-C₁₂ monovalent hydrocarbon radical, a C₁-C₁₂ monovalent hydrocarbon radical containing ether linkages, a halogen-substituted C₁-C₁₂ monovalent hydrocarbon radical, and a halogen-substituted C₁-C₁₂ monovalent hydrocarbon radical containing ether linkages.

4. The copolymer of claim 1, wherein said POSS monomer has a closed-cage structure.
5. The copolymer of claim 1, wherein said POSS monomer has an open-cage structure.
6. The copolymer of claim 1, further comprising
 - a) the POSS monomer at about 3 to about 25 weight percent;
 - b) the ethylenically unsaturated, monofunctional organosiloxane monomer at about 2 to about 60 weight percent;
 - c) the hydrophilic monomer at about 1 to about 25 weight percent;
 - d) a hardness modifying (meth)acrylate monomer at 0 to about 50 weight percent; and
 - e) a non-silicone containing crosslinking agent at 0 to about 20 weight percent.

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 June 2002 (27.06.2002)

PCT

(10) International Publication Number
WO 02/050144 A3

(51) International Patent Classification⁷: C08F 230/08,
G02B 1/04

(21) International Application Number: PCT/US01/46500

(22) International Filing Date: 3 December 2001 (03.12.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/256,712 19 December 2000 (19.12.2000) US

(71) Applicant: BAUSCH & LOMB INCORPORATED
[US/US]; One Bausch & Lomb Place, Rochester, NY
14604-2701 (US).

(72) Inventors: BONAFINI, Jr., James, A.; 15 Park View
Drive, Pittsford, NY 14604-2701 (US). SALAMONE,
Joseph, C.; 740 NW 6th Street, Boca Raton, FL 33486
(US).

(74) Agents: POLYN, Denis, A. et al.; One Bausch & Lomb
Place, Rochester, NY 14604-2701 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA,
ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG).

Declaration under Rule 4.17:

— as to the identity of the inventor (Rule 4.17(i)) for the fol-
lowing designations AE, AG, AL, AM, AT, AU, AZ, BA, BB,
BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK,
DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent
(GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
TG)

Published:

— with international search report

(88) Date of publication of the international search report:
16 January 2003

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

WO 02/050144 A3

(54) Title: POLYMERIC BIOMATERIALS CONTAINING SILSESQUOXANE MONOMERS

(57) Abstract: The invention provides a biocompatible copolymer produced by polymerizing a mixture comprising at least one monomer selected from the group consisting of itaconates, (meth)acrylates, fumarates and styrenics, at least one ethylenically unsaturated organosiloxane monomer and at least one monomer comprising a POSS compound.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/46500

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C08F230/06 G02B1/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C08F G02B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHEMICAL ABSTRACTS, vol. 96, no. 20, 17 May 1982 (1982-05-17) Columbus, Ohio, US; abstract no. 163657, "SILICONE COMPOUNDS" page 35; column 2; XP002210095 abstract & JP 82 012057 A (HITACHI CHEM. CO. LTD) 21 January 1982 (1982-01-21)	
A	US 4 743 667 A (Y. MIZUTANI) 10 May 1988 (1988-05-10) cited in the application	
A	US 5 412 053 A (J. LICHTENHAN) 2 May 1995 (1995-05-02) cited in the application	

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *G* document member of the same patent family

Date of the actual completion of the international search

16 August 2002

Date of mailing of the international search report

02/09/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Cauwenberg, C

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/46500

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 82012057	A	NONE	
US 4743667	A	10-05-1988	JP 1020408 B 17-04-1989 JP 1586181 C 31-10-1990 JP 62054220 A 09-03-1987
US 5412053	A	02-05-1995	US 5484867 A 16-01-1996 US 5589562 A 31-12-1996

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☒ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.